REMARKS/ARGUMENTS

Status of the Claims

Prior to entry of this amendment Claims 107-112, 115, 117, 119-120 were pending. Claims 107-110, 115, 117 and 120 are amended. Support is found throughout the specification and in the claims as filed. The amendments specify that the fucosyltransferase VI and VII are human fucosyltransferases. Support is found throughout the specification and at least on p. 26, lines 5-10. Applicants request entry of this amendment as the amendments serve to place the claims in condition for allowance or better condition for appeal.

Applicants appreciate the Examiner withdrawing the prior rejections under 35 U.S.C. § 112, first paragraph and 35 U.S.C. §102.

Objection

Claims 108-112, 119 and 120 are objected to as allegedly being in improper form. The claims depend from claims 107, 115 or 117, which, according to the Examiner, are multiple dependent claims depending on dependent claims 115 and 117. Applicants traverse. It is true that a multiple dependent claim shall not serve as a basis for any other multiple dependent claim. However, we note that claims 115 and 117 are not multiply dependent claims, in contrast to the Examiner's characterization. Rather, claim 115 only depends from claim 107 and claim 117 only depends from claim 115. In view of this, Applicants request the Examiner to withdraw this objection and confirm that claims 108-112, 119 and 120 are being examined.

Rejection Under 35 U.S.C. §112

Claims 107-112, 115, 117, 119 and 120 are rejected under 35 U.S.C. 112, first paragraph as allegedly lacking enablement. The Examiner asserted that the specification does not enable "any method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for any recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase...wherein said recombinant FucT-VI or FucT-VII provides at least 2-, 4- or

8-fold greater fucosylation of said glycopeptides than is achieved under identical conditions using any FucT-V either naturally derived by biochemical means or recombinantly produces FucT-V." The Examiner also suggested that the specification did not enable the full scope of the claims. Specifically, the Examiner stated "In light of the above teachings a skilled artisan requires the structure and the source of the fucosyltansferase especially when activities are being compared." Applicants respectfully traverse the rejection.

While Applicants do not necessarily agree with the propriety of the rejection, the claims have been amended in an effort to expedite prosecution of this application. Thus, as amended, the claims are directed to methods

> wherein said fucosyltransferase is an isolated, recombinantly produced human FucT-VI or human FucT-VII fucosyltransferase wherein said fucosyltransferase lacks a membrane anchoring domain, and wherein said fucosyltransferase provides at least 2-fold greater fucosylation of said glycopeptide than is achieved under identical conditions using recombinant, isolated FucT-V.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).* Furthermore, a patent need not teach, and preferable omits, what is well known in the art. *In re Butcher, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed Cir. 1991; Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).* The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).* The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). See also, MPEP § 2164.01.*

As noted above, in the spirit of expediting prosecution, Applicants have amended the claims. As amended, the claims are directed to methods wherein the FucT-VI and FucT-VII are human fucosyltransferases. The Applicants note that the specification provides ample disclosure to enable one skilled in the art to practice the claimed invention. For example, the specification provides working examples (Examples 2 and 3) showing the results of the substrate specificity and fucosylation activity of the fucosyltransferases.

Moreover, methods of determining whether an intended FucT-VI or FucT-VII fucosyltransferase-mediated modification occurred are readily accessible to, and well within the abilities of, those of skill in the art. Therefore, in view of the guidance provided in the specification, in combination with the knowledge of one of skill in the art, any experimentation that may be performed is reasonable in scope and cannot be properly characterized as "undue".

In summary, the specification clearly teaches that FucT-VI or FucT-VII can be used *in vitro* to provide a substantially uniform fucosylation pattern for glycopeptides. The specification also provides ample examples to demonstrate the operability and success of the claimed methods achieved by following the teaching and guidance provided by the present invention. Therefore, the Applicants respectfully request that this rejection be withdrawn.

Claims 107-112, 115, 117, 119 and 120 are rejected under 35 U.S.C. 112, first paragraph as allegedly lacking written description. As noted above, the Examiner stated "In light of the above teachings a skilled artisan requires the structure and the source of the fucosyltansferase especially when activities are being compared." Applicants respectfully traverse the rejection.

Notably, as noted previously, Applicants have amended the claims such that they are directed to methods wherein the FucT-VI and FucT-VII are human fucosyltransferases. Applicants respectfully submit that the claimed *in vitro* methods are directed to the use of a group of well known enzymes, *i.e.,* fucosyltransferases, which are adequately described in the specification. Moreover, as has also been acknowledged during the prosecution of this

application, the sequence information of fucosyltransferases is well known and publicly available. Therefore, by identifying the enzyme, *i.e.,* human fucosyltransferase VI and VII and by providing structural descriptions, *e.g.,* lacking membrane anchoring domain, the specification clearly describes the fucosyltransferases useful for the claimed methods.

It has long been held by the court that what is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See MPEP 2163 IIA 3(a) and *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. See, *e.g., Vas-Cath*, 935 F.2d at 1563, 19 USPQ2d at 1116.

Applicants respectfully submit that, in addition to the detailed descriptions provided by the specification, the examples provided by the specification further demonstrate that the inventors of the present invention were in possession of the claimed invention at the time of filing. Specifically, in Example 2, the inventors demonstrated that while both FucT-VI and FucT-V could be used for *in vitro* glycosylation according to the methods taught by the present invention, FucT-VI was capable of incorporating approximately 8-fold more fucose than FucT-V. Example 3 demonstrate that fucosylation by FucT-VI *in vitro* can be proceed by a sialylation step as taught by the present invention. Therefore, the description and examples provided by the specification at the time of filing clearly show that the inventors were in possession of the method as claimed. Applicants respectfully request the Examiner to withdraw the rejection.

Rejection Under 35 U.S.C. §103

Claims 107-112, 115, 117, 119 and 120 are rejected under 35 U.S.C. 103 as being unpatentable over Lowe JB[1] (U.S. Patent 5,324,663 ('663)) or Lowe[2] (U.S. Patent 5,770,420 ('420)) or Lowe JB[3] (U.S. Patent 6,268,193) or Sasaki et al., (U.S. Patent No. 7,094,530) and in view of de Vries et al., (J. Biol Chem., 1995, Vol. 270 (15): 8712-8722), Seed. B., (WO

96/40881), Rasko et al., (J. Biol. Chem., 2000, Vol. 275 (7): 4988-4994), Staudacher E., (Trends Glycosci and Glycobiol., 1996 Vol. 8 (44): 391-408), Malissard et al. (BBRC 2000, Vol. 267: 169-173) and Prieels et al., (J. Biol. Chem.,, vol. 256 920): 10456-10463). Applicants respectfully traverse.

As noted previously, the law is clear that to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones,* 21 USPQ2d 1941 (Fed. Cir. 1992). Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 231 USPQ 375 (Fed. Cir. 1986). Third, the prior art reference, or references when combined, must teach or suggest all the claim limitations. *In re Royk*a, 180 USPQ 580 (CCPA 1974).

In affirming the obviousness analysis that it had set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), the Supreme Court has also stated that "[t]here is no necessary inconsistency between the idea underlying the TSM [i.e., teaching-suggestion-motivation] test and the *Graham* analysis." *KSR Int'l Co. v. Teleflex Inc.*, No. 04-1350, slip op. at 13 (2007). Thus, the Supreme Court has not invalidated the TSM test, but rather only rejected its "rigid" application. *See id.* at 11. An obviousness rejection continues to require an explicit analysis providing some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. *See id.* at 14 (citing *In re Kahn*, 411 F.3d 977, 988 (Fed. Cir. 2006)).

The alleged *prima facie* case of obviousness here is deficient because the cited references alone, or in any combination, fail to teach each and every element found in the claims. In particular, the combination of references fails to a method that requires transfer of fucose by isolated, recombinantly produced human FucT-VI or FucT-VII to a recombinant polypeptide...wherein the fucosyltransferase provides at least 2-fold greater fucosylation of the glycopeptide than is achieved under identical conditions using recombinant, isolated FucT-V. This is in contrast to the Examiner's statement that "The cited prior art provides ample

guidance with respect to all the elements of the instant invention." There is simply no discussion in any of the cited references of a method in which human FucT-VI or FucT-VII "provides at least 2-fold greater fucosylation of said glycopeptide than is achieved under identical conditions using recombinant, isolated FucT-V". Accordingly, because each claim limitation is not disclosed in the cited references, either alone or in combination, Applicants submit that the alleged prima facie case of obviousness is in error.

Applicants maintain that one of skill in the art would not have had a reasonable expectation of success in practicing the invention as claimed based on the teachings of the cited references. As the Examiner noted, enzymatic activities of fucosyltransferases are varied and unpredictable. Prior to the instant application one of skill in the art would not have had a reasonable expectation of success in practicing the invention in which human FucT-VI or FucT-VII "provides at least 2-fold greater fucosylation of said glycopeptide than is achieved under identical conditions using recombinant, isolated FucT-V". This surprising and unexpected result is highlighted in the specification:

> As most of the studies on in vitro fucosylation to date have focused on the fucosylation of small molecule substrates, the art has not recognized any substantial difference between the efficiency of fucosylation of the various fucosyltransferases. The inventors have, however, discovered that certain FucT molecules are *surprisingly more effective at fucosylating glycopeptides*. For example, FucT-VI is approximately 8-fold more effective at fucosylating glycopeptides than is FucT-V. Thus, in a preferred embodiment, the invention provides a method of fucosylating an acceptor on a glycopeptide using a fucosyltransferase that provides a degree of fucosylation that is at least about 2-fold greater, more preferably at least about 4-fold greater, still more preferably at least about 6-fold greater, and even more preferably at least about 8-fold greater than is achieved under identical conditions using FucT-V. Presently preferred fucosyltransferases include FucT-VI and FucT-VII. (Emphasis added) (See page 26, line 9 to page 27, line 2.)

Accordingly, Applicants submit that prior to the instant application one of ordinary skill in the art would not have had a reasonable expectation of success in practicing the invention as claimed.

In view of the above, Applicants submit that the combination of references fails to teach each of the limitations of the claims. Moreover, one of skill in the art would not have

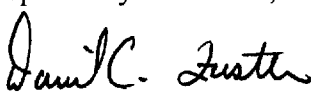
had a reasonable expectation of success in practicing the method as claimed. As such, there is no *prima facie* case of obviousness. Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants respectfully request a telephone interview if the Examiner believes that the claims as amended are not in condition for allowance in light of the response submitted above. The undersigned can be reached at 415-442-1000.

Respectfully submitted,



David C. Foster
Reg. No. 44,685

MORGAN, LEWIS & BOCKIUS, LLP
One Market, Spear Street Tower
San Francisco, California 94105
Direct Dial: 415.442.1216
Tel: 415.442.1000
E-Fax: 415.442.1001
e-mail: david.foster@morganlewis.com

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